

In the Claims

This listing of claims will replace all previous versions and listings of claims in the application:

1. (Original) A process for controlling the amount of sialic acid present on an oligosaccharide side chain of a glycoprotein produced by mammalian cell culture which comprises:
culturing the mammalian host cell in a production phase of the culture which is characterized by;
 - i) adding an alkanoic acid or a salt thereof to the cell culture at a concentration of about 0.1 mM to about 20 mM; and
 - ii) maintaining the osmolality of the cell culture at about 250 to about 600 mOsm.
2. (Original) The process according to claim 1 wherein the amount of sialic acid present on the oligosaccharide side chain of the glycoprotein is increased and wherein;
cell specific productivity of the cell culture is decreased by culturing the host cell at a concentration of the alkanoic acid or salt thereof of about 0.1 to about 6mM and maintaining the osmolality at about 300-450 mOsm.
3. (Original) The process of claim 2 in which the host cell is a CHO cell.
4. (Original) The process according to claim 3 wherein the alkanoic acid or salt thereof is sodium butyrate.
5. (Original) The process according to claim 4 wherein the glycoprotein produced is a mammalian glycoprotein.
6. (Original) The process according to claim 5 wherein the glycoprotein is a tumor necrosis factor receptor-immunoglobulin chimera.
7. (Original) The process of claim 6 in which the host cell is a dp12.CHO cell line transfected with the vector carrying the cDNA encoding a soluble type 1 tumor necrosis factor immunoglobulin G₁ chimera.

8. (Original) The process according to claim 1 wherein the amount of sialic acid present on the oligosaccharide side chain of the glycoprotein is decreased and wherein; cell specific productivity of the cell culture is increased by culturing the host cell at a concentration of about 6mM to about 12 mM of the alkanolic acid or salt thereof and maintaining the osmolality at about 450-600 mOsm.
9. (Original) The process of claim 8 in which the host cell is a CHO cell.
10. (Original) The process according to claim 9 wherein the alkanolic acid or salt thereof is sodium butyrate.
11. (Original) The process according to claim 10 wherein the glycoprotein produced is a mammalian glycoprotein.
12. (Original) The process according to claim 11 wherein the glycoprotein is a tumor necrosis factor receptor-immunoglobulin chimera.
13. (Original) The process of claim 14 in which the host cell is a dp12.CHO cell line cell transfected with the vector carrying the cDNA for a soluble type 1 tumor necrosis factor immunoglobulin G₁ TNFR1-IgG₁ chimera.
14. (Original) A process for producing a tumor necrosis factor receptor-immunoglobulin TNFR1-IgG₁ chimeric protein comprising;
 - (a) culturing a mammalian host cell which expresses a TNFR-IG chimera in a growth phase under such conditions and for a period of time such that maximum cell growth is achieved;
 - (b) culturing the host cell in a production phase in the presence of sodium butyrate at a concentration of about 6mM to about 12 mM;
 - (c) maintaining the osmolality of the production phase at about 450-600 mOsm.
15. (Original) A process for producing a tumor necrosis factor receptor-immunoglobulin TNFR1-IgG₁ chimeric protein comprising;

- (a) culturing a mammalian host cell which expresses a TNFR-IG chimera in a growth phase under such conditions and for a period of time such that maximum cell growth is achieved;
 - (b) culturing the host cell in a production phase in the presence of sodium butyrate at a concentration of about 1mM to about 6 mM;
 - (c) maintaining the osmolality of the production phase at about 300-450 mOsm.
16. (Original) The process of claim 15 in which the host cell is a CHO cell.
17. (Original) The process of claim 16 in which the host cell is a dp12.CHO line.
18. (Original) A preparation comprising the TNFR1-IgG₁ produced by the process of claim 17.
19. (Original) A therapeutic composition comprising the TNFR1-IgG₁ produced by the process of claim 15, and a pharmaceutically acceptable excipient.
20. (Currently amended) A ~~TNFR1-IgG₁~~ human TNFR1-IgG₁ preparation comprising ~~TNFR1-IgG₁~~ human TNFR1-IgG₁ molecules wherein the ~~TNFR1-IgG₁~~ TNFR1-IgG₁ molecules have a molar ratio of sialic acid to protein of about 4-7.
21. (Currently amended) A ~~TNFR1-IgG₁~~ TNFR1-IgG₁ preparation comprising ~~TNFR1-IgG₁~~ TNFR1-IgG₁ molecules wherein the ~~TNFR1-IgG₁~~ TNFR1-IgG₁ molecules have about 1-2 moles of exposed N-acetylglucosamine residues per mole of ~~TNFR1-IgG₁~~ TNFR1-IgG₁ protein.
22. (Currently amended) A ~~TNFR1-IgG₁~~ TNFR1-IgG₁ preparation comprising ~~TNFR1-IgG₁~~ TNFR1-IgG₁ molecules wherein the ~~TNFR1-IgG₁~~ TNFR1-IgG₁ molecules have a molar ratio of sialic acid to N-acetylglucosamine of about 0.35 to about 0.5.
23. (Currently amended) The ~~TNFR1-IgG₁~~ TNFR1-IgG₁ preparation of claim 22 wherein the molar ratio of sialic acid to N-acetylglucosamine is about 0.39 to about 0.45.